



## Comment on case series of COVID-19 in patients with myasthenia gravis: a single institution experience by Županić et al.

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Županić et al. [1] described eight patients, six males and two women, with pre-existing diagnosis of myasthenia gravis (MG) and COVID-19 infection. In four cases, acetylcholine receptor (AChR) antibodies were detected, while two were seronegative, and the remaining untested. Interestingly, at the time of the SARS-CoV-2 infection, three cases were asymptomatic, whereas one was in stage 1, two in stage 2b, and one in stage 3b according to Myasthenia Gravis Foundation of America score (MGFA) [2]. The authors [1] stated that four patients (case 1, 2, 4, 7) showed clear-cut worsening symptoms of MG on admission, but apparently only two of those (case 4 and 7) exhibited a deepening in MGFA severity; in one case (8) who was admitted because of respiratory failure, after fever, cough and dyspnea, the neurological assessment was inconclusive. Pneumonia was reported in six; among those, four received remdesivir added to dexamethasone in one and dexamethasone alone in another. Out of the eight, non-invasive oxygen therapy was applied in two: case 3, asymptomatic during hospital stay and 7 who was classified as 2b in MGFA score. In such patients, we would consider the need of respiratory support due to the SARS-CoV-2 pneumonia. Interestingly, only one patient (case 4) showed a myasthenic crisis (MC) which needed mechanical ventilation (MV). Death occurred only in one patient, who died after 11 days of intensive-care unit (ICU), while the remaining had fair outcome. Six patients of Županić et al. [1] received intravenous immunoglobulins (IVIG) at usual dose, eventually added to their baseline

therapy. The description of this case series is interesting and deserves a brief comment.

First, while for other neurological manifestations of central nervous system, it can be easy to establish a relation with COVID-19, in case of neuromuscular disorders, clinicians must be cautious in attributing the symptoms to worsening of the neurological status rather than to the COVID-19 itself [3, 4]. About 20% of patients with SARS-CoV-2 exhibit respiratory weakness and failure, due to viral infection [5]. The development of selective respiratory muscles weakness could be a feature of COVID-19-related MG exacerbation, and may be triggered by increased inspiratory effort due to respiratory drive activation in the course of concurrent pneumonia [4]. In this scenario, early non-invasive pressure support could prevent fatigue and potentially avoid the need for MV in patients without significant alterations in gas exchange. Indeed, endotracheal intubation and MV, despite being the gold standard of treatment for acute respiratory failure due to MC, are associated with complications, including pneumonia and atelectasis, as well as prolonged ICU stays and difficult weaning [6]. Furthermore, some retrospective studies show that about 40% or more of MC patients undergoing MV fail weaning trial and require tracheostomy [6].

Second, Županić et al. [1] do not provide details about severity of the concurrent pneumonia and radiological results; these data could clarify the interplay between MG and COVID-19 infection. Also, a functional respiratory muscle assessment might help to identify the development of weakness and the timing of initiation of non-invasive ventilation. However, given the fluctuating nature of muscle fatigue typical of MG, the respiratory functional assessment may also not be able to predict the need of ventilatory support.

Third, we think that the decisions on management of patients with generalized MG and SARS-CoV-2 infection

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should be taken thorough careful neurological surveillance. A cautious administration of IVIG is recommended in patients with concomitant SARS-CoV-2 infection, because widespread thrombosis has been reported in critically ill COVID-19 patients, as previous authors pointed out [1, 5, 7]. According to the literature, the IVIG treatment or plasma exchanges should be introduced in MG in case of clear-cut acute exacerbations of respiratory and neurological symptoms and in conditions defined as MC [6, 7]. The rationale of the use of IVIG should be a short-term treatment in patients with life-threatening signs or when a rapid clinical response is needed or when other therapies are insufficiently effective [6, 7]. Finally, the Brazilian series [8] with 30% rate of death in MG hospitalized with COVID-19 describes patients with features falling into the definition of MC, as 87% were admitted to ICU and 73% needed MV.

## Declarations

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** This article does not contain any studies with human participants or animals performed by any of the authors.

**Informed consent** Informed consent was obtained from all individual participants included in the study.

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